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EXAMINER

PRIEBE, SCOTT DAVID

ART UNIT	PAPER NUMBER
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1632

DATE MAILED: 09/03/2002

14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/647,377

Applicant(s)

ROSENTHAL ET AL.

Examiner

Scott Priebe

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 June 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-28 is/are pending in the application.
- 4a) Of the above claim(s) 9-11, 14-19, 22, 27 and 28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7, 20, 21 and 23-26 is/are rejected.
- 7) ☒ Claim(s) 8, 12 and 13 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 12 February 2001 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

Art Unit: 1632

DETAILED ACTION***Election/Restriction***

Applicant's election with traverse of Group I, directed to the murine LOBO, in Paper No. 12 filed 6/18/02 is acknowledged. The traversal is on the ground(s) that SEQ ID NOs 8 and 13 encode the same protein, and groups I and II should be rejoined. This is not found persuasive because according to the specification (including the Sequence Listing) SEQ ID NO: 8 is a cDNA sequence obtained from a mouse encoding murine LOBO, whereas SEQ ID NO: 13 is hypothetical coding sequence for part of the human LOBO assembled from human genomic sequences (see also page 26). As shown in Figs. 2a-2m, the human LOBO is not the same protein as the murine LOBO, for example it is shorter by 387 amino acids. Furthermore, if inactivation of human LOBO is responsible for AHO, as speculated upon in Example 7, then the sequences encoding human LOBO do not appear to meet the functional limitation of claim 1, that reduction or inactivation of the protein result in long bones. AHO has a very different phenotype, i.e. short bones and obesity. No traversal of the restriction between groups I- II versus groups III-XIV has been presented.

The requirement is still deemed proper and is therefore made FINAL.

Claims 9-11, 14-19, 22, 27 and 28 in their entirety and claims 1-8, 12, 13, 20, 21, and 23-26 as directed to SEQ ID NOs 13 and 14 are withdrawn from further consideration pursuant to 37

Art Unit: 1632

CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 12.

Drawings

The drawings are objected to for the reasons set forth in the attached PTO-948. Corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Specification

The disclosure is objected to because of the following informalities:

The description of Figures 2 and 3 (page 16) do not correspond to Figures 2a-2m and 3. There is no "Figure 2" *per se*. The description of Fig. 2 appears to be of the subject matter shown in Fig. 3 While the description of Fig. 3 appears to be directed to Figures 2a-2m.

Page 24 describes the cloning and sequencing of the murine genomic sequence. At line 9, it states that SEQ ID NOs; 12-15 give murine genomic sequence. However, according to the Sequence Listing of these only SEQ ID NO: 12 is murine sequence; SEQ ID NOs: 13-15 are directed to human sequences.

Appropriate correction is required.

Art Unit: 1632

Claim Objections

Claims 8, 12, and 13 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim must refer to other claims in the alternative only. Claim 8 depend from both claims 1 and 7, but not alternatively. Claims 12 and 13 depend from a series of claims in both the alternative and together by reciting "and/or". See MPEP § 608.01(n). Accordingly, the claims 8, 12 and 13 have not been further treated on the merits.

Claim Rejections - 35 USC § 101 & 112

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, and 4 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims do not require that the nucleic acid molecule be isolated from its natural milieu. Consequently, the claims embrace nucleic acid molecules that exist in a living mouse, e.g. the mouse gene and the mRNA expressed from the gene. This

Art Unit: 1632

rejection would be overcome by inserting "isolated" before "nucleic acid molecule" in line 1 of claim 1.

Claims 1-7, 20, 21, 23-26 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The elected invention is directed to nucleic acid molecules comprising a nucleic acid sequence that 1) hybridizes to a nucleic acid sequence encoding SEQ ID NO: 9 (murine LOBO protein) and that encodes a protein, the reduction or elimination of which in an animal results in longer bones. The only asserted uses for the nucleic acid molecules is in diagnosis or treatment of an undisclosed disease or to make the protein encoded thereby (which in turn can be used to make antibodies to the protein) which can be used in diagnosis or treatment.

The specification (page 1) discloses that a number of hereditary diseases resulting in impaired growth and development of bone are known. However, the exact genetic factors are unknown, and diagnostic and treatment methods are in most cases unavailable. However, the specification fails to identify a single disease of any kind, including a disease involving bone growth and development, that could either be diagnosed or treated with a nucleic acid molecule of the invention, or with a protein or antibody made using the nucleic acid. In order to practice these uses of the invention, one of skill in the art would first be required to determine if there is a disease that could be either diagnosed or treated with the claimed invention (or products made

Art Unit: 1632

with it), and then determine how to use it for that purpose. Potentially any nucleic acid molecule encoding any protein (or the protein or antibody) can be used to identify a disease that can be either diagnosed or treated with the nucleic acid molecule, albeit the potential success in such endeavors would differ depending on the protein or nucleic acid. Such use constitutes nothing more than further research on the invention itself in order to determine a use for the invention, and is neither a specific nor substantial use of the claimed invention. *Brenner v. Manson*, 148 USPQ 689, 695-696 (US SupCt., 1966).

The possible involvement of the LOBO in bone growth, and potentially in mitosis and cell-cycle control would clearly make LOBO an attractive subject of further scientific inquiry. However, using an invention for the purpose of expanding scientific knowledge of the invention, and, in so doing scientific knowledge of any processes it is involved in, is not a utility that meets the requirements of § 101. See *Brenner* at 695-696.

Claims 1-7, 20, 21, 23-26 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 1-7, 20, 21, 23-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey

Art Unit: 1632

to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The elected invention is directed to a nucleic acid sequence encoding SEQ ID NO: 9 (including that of SEQ ID NO: 8) which is named by the inventors as murine LOBO protein, and any generic nucleic acid sequence whose complement hybridizes to a sequence encoding murine LOBO and encodes a protein, the reduction or inactivation of which in an animal causes bones, except for the skull, to become longer. The protein encoded by the claimed nucleic acid is defined solely by the phenotype conferred by its absence or reduction in an animal, specifically in an animal that has bones. Consequently, the protein encoded by a nucleic acid sequence of the invention must be a protein found naturally in an animal that has bones.

The specification discloses only one amino acid sequence, SEQ ID NO: 9, which clearly meets the phenotype limitation of the claims. The specification discloses a partial amino acid sequence for a human homolog of murine LOBO (SEQ ID NO: 14), however, the specification provides no evidence that loss or reduction of this human protein would lead to longer bones in a human. The specification in Example 7 speculates on whether the human homolog of murine LOBO is a candidate gene for Albright hereditary osteodystrophy (AHO) in humans. However, the phenotype of AHO is hyposomia (inadequate development of the body), obesity, and brachydactylia (short fingers). i.e. short bones not long bones. The specification acknowledges that the same mutation in a mouse gene and a human gene “can lead to quite different

Art Unit: 1632

phenotypes” (page 31). Consequently, the specification does not unequivocally teach that a nucleic acid sequence encoding human LOBO meets the phenotype limitation of the claim.

The claims are directed to a genus of polynucleotide encoding a generic protein. Only one species of protein clearly meeting the requirements of the claims has been described by its complete structure, i.e. a nucleic acid sequence encoding SEQ ID NO: 9. The specification discloses that eukaryotic DIS3 proteins and a LOBO homolog of *C. elegans* as well as VACB and RNAase II proteins of bacteria and fungi are structurally homologous to LOBO (Figs. 2a-2m and 6). However, the specification discloses that these proteins have functions different than LOBO; a reduction or elimination of their activity would not cause longer bones. The specification does not describe any biological function or biochemical activity for LOBO proteins, nor any assay for LOBO function or activity that could be used to distinguish a LOBO protein from any other protein, particularly from those potential which are structurally similar to LOBO but having a different function, such as the DIS3, VACB and RNAase II proteins. Structural homologs of non-vertebrates, e.g. bacteria, fungi, and nematodes clearly do not meet the limitations of the claims as these organisms have no bones. As indicated above, it is not clear that the human LOBO would meet the phenotype limitation of the claims. The specification does not disclose any structural features that would distinguish the claimed nucleic acid molecules from those encoding structurally similar, but functionally different proteins meeting the hybridization limitation.

Art Unit: 1632

In addition, the claims are directed solely to nucleic acid sequences encoding a naturally occurring protein. The claims do not embrace nucleic acid sequences meeting the hybridization limitation that encode a non-natural protein that could substitute functionally for the naturally occurring LOBO of a given animal. The specification does not identify any structural features of a naturally occurring protein that would distinguish it from a man-made protein of similar structural and identical function. For example, if one of skill in the art were given a nucleic acid sequence encoding a protein structurally similar to murine LOBO, and functionally identical to murine LOBO, that one of skill would be unable to determine whether the protein was a natural LOBO protein or a purely artificial homolog.

Also, the claims in general and claims 2 specifically are directed to genomic DNA encoding the protein. The specification does not disclose a single genomic DNA readable on the claims. The specification describes partial genomic sequences from the murine LOBO gene, and freely admits that additional genomic sequences remain, specifically the 5' end of the gene corresponding to the 5' non-transcribed sequences including the promoter, transcribed sequences which correspond to nucleotides 1-1242 of the mRNA (page 25). Thus the specification clearly indicates that applicant was not in possession of the genomic DNA encoding a LOBO protein.

The court and the Board have repeatedly held (*Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (CA FC, 1991); *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993); *Fiddes v. Baird*, 30 USPQ2d 1481 (BPAI 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)) that an adequate written description of a nucleic acid requires

Art Unit: 1632

more than a mere statement that it is part of the invention and reference to a potential method for isolating it, irrespective of the complexity or simplicity of the method; what is required is a description of the nucleic acid itself. It is not sufficient to define DNA solely by its principal biological property, because disclosure of no more than that is simply a wish to know the identity of any DNA with that biological property. Naming a type of material generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. When one is unable to envision the detailed constitution of a complex chemical compound having a particular function, such as a nucleic acid, so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e., until after the nucleic acid has been isolated. Thus, claiming all DNA's that achieve a result without defining what means will do so is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. Also, where a claim purports to cover all nucleic acids that encode a specific protein and the specification discloses but a single DNA known to do so, the situation is analogous to a single means claim and does not meet the enablement requirement under para. 1 of §112.

This rejection would be overcome by limiting the claims to a nucleic acid sequence encoding SEQ ID NO: 9.

Claim Rejections - 35 USC § 102

Art Unit: 1632

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4, 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Browning et al. (Proc. Natl. Acad. Sci. USA 94: 14637-14641, 1997).

The claims are directed to a nucleic acid molecule, genomic DNA or RNA, or a cell “transformed with” the nucleic acid molecule. Claims 1, 2 and 4 do not require that the nucleic acid molecule be isolated. Therefore, these claims embrace any naturally occurring genomic DNA or mRNA encoding murine LOBO in its natural location. The specification discloses that the LOBO mRNA is ubiquitously expressed, i.e. it is expressed in all mouse cells. With respect to claim 7, a mouse cell made by transforming with the genomic DNA could result in a mouse cell indistinguishable from the untransformed cell if the input genomic DNA underwent homologous recombination with the mouse genome. Transformation of the mouse cell with LOBO mRNA would simply add more LOBO mRNA to the endogenous pool of LOBO mRNA. In either case, the resulting mouse cell would be indistinguishable from a mouse cell that had not been transformed.

Browning et al. discloses the mouse cell line 3T3, FVB and C57/B6 mice and a transgenic mouse with FVB and C57/B6 parents and cells removed from the transgenic mouse.

Art Unit: 1632

Since the LOBO gene and mRNA expressed therefrom are inherent characteristics of a mouse or mouse cell, the genomic DNA and mRNA in the mice and cells disclosed by Browning et al. anticipate the claims.

The rejection of claims 1, 2 and 4 would be overcome by limiting the claims to --isolated- nucleic acid molecules. The rejection of claim 7 would be overcome by directing the claims to host cells transformed with the vector of claims 5 or 6, rather than a generic nucleic acid molecule.

Certain papers related to this application may be submitted to Art Unit 1632 by facsimile transmission. The FAX numbers are (703) 308-4242 or (703) 305-3014 for any type of communication. In addition, FAX numbers for a computer server system using RightFAX are also available for communications before final rejection, (703) 872-9306, and for communications after final rejection, (703) 872-9307, which will generate a return receipt. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe whose telephone number is (703) 308-7310. The examiner can normally be reached on Monday through Friday from 8 AM to 4 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051.

Any inquiry concerning administrative, procedural or formal matters relating to this application should be directed to Patent Analyst Patsy Zimmerman whose telephone number is (703) 308-8338. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.



Scott D. Priebe, Ph.D.
Primary Examiner